

**EDTN
HPV TEST PLAN**

Submitted to the U.S. Environmental Protection Agency

By

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SUMMARY

Akzo Nobel Functional Chemicals LLC has sponsored ethylenediaminetetraacetonitrile (CAS# 5766-67-6), also known as EDTN, in the U.S. EPA High Production Volume (HPV) program. Although there are no experimental data on SIDS endpoints for EDTN, data exists on these endpoints for propylenediaminetetraacetonitrile (CAS# 110057-45-9), also known as PDTN and an analog of EDTN.

Robust summaries of studies on PDTN and EDTN are included in this submission. Data on EDTN from the EPIWIN computer model were used in the absence of experimental values on PDTN for boiling point, photodegradation and fugacity. EDTN data were also used to compare with PDTN experimental values for other environmental chemistry endpoints to show similarities between the two chemicals and support the use of PDTN data for mammalian toxicity and ecotoxicity endpoints. The table below summarizes the endpoints of interest in the HPV program, the available data, and indicates proposed testing.

| Endpoint | Data Available & Sufficient | Testing Proposed |
|-----------------------------------|--|-------------------------|
| Physical/Chemical Characteristics | Yes | No |
| Photodegradation | Yes | No |
| Hydrolysis | Yes | No |
| Biodegradation | Yes | No |
| Transport | Yes | No |
| Acute Fish Toxicity | Yes | No |
| Acute Daphnia Toxicity | Yes | No |
| Acute Alga Inhibition | Yes | No |
| Acute Toxicity | Yes | No |
| Genetic Toxicity | Yes | No |
| Repeated Dose | Yes | No |
| Reproductive Toxicity | No | Yes (OECD 421) |
| Developmental Toxicity | No | Yes (OECD 421) |

1.0 INTRODUCTION

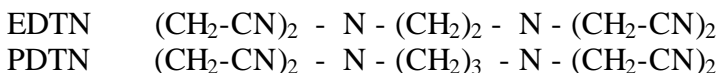
Akzo Nobel Functional Chemicals LLC has sponsored EDTN (CAS# 5766-67-6) in the U.S. HPV program to assess its health and environmental hazards, including selected physical/chemical characteristics. In the absence of data on EDTN, data on the structurally similar chemical, PDTN (CAS# 110057-45-9), will be used.

This document includes justification for the use of PDTN data. The justification for this is based on similarities in chemical structure, physical/chemical properties and metabolism between EDTN and PDTN. In addition, an evaluation of the available toxicity data and proposed test plan are included.

It is proposed that water solubility and vapor pressure studies and a reproductive/developmental toxicity screening study (OECD 421) be conducted on EDTN.

2.0 PDTN: AN ANALOG

The structures of EDTN and PDTN are seen below.



The structures show that the only difference is that PDTN has one more carbon atom between the two nitrogens. Both chemicals have four identical acetonitrile groups which determine the function and reactivity of EDTN and PDTN. Due to the similarity, it is not unexpected that EDTN and PDTN have similar physical/chemical properties. Both are white solids with similar solubility in many types of solvents and have the same thermographic analysis curve. In addition, EDTN and PDTN react almost identically with water, ammonia, alkali, hydrogen and halogens.

The difference in synthesis of EDTN and PDTN is that 1,3 propylenediamine is used for PDTN unlike 1,2 ethylenediamine as described for EDTN above. Table 1 compares the physical/chemical properties of EDTN and PDTN.

The similarity in structure, physical/chemical properties and reactivity suggests that the metabolism of EDTN and PDTN will be the same. In both cases, the bond between nitrogen atom and carbon atoms (N-CH₂-CN) can be broken by hydrolysis whereas the bridge, (N-(CH₂)₂-N) or (N-(CH₂)₃-N), is very stable. Therefore, the additional carbon atom in PDTN is not expected to change its metabolism relative to EDTN. The same metabolic pathway of EDTN and PDTN indicates that the toxicity profile of these structurally similar chemicals is expected to be the same. Therefore, the use of PDTN toxicity data for EDTN data gaps should be acceptable.

3.0 EVALUATION OF EXISTING DATA AND PROPOSED TESTING

The available data for PDTN and EDTN have been evaluated below and summarized in Tables 1-3. Since there are no experimental data on EDTN, the experimental data are only from studies on PDTN. Data on EDTN from the EPIWIN computer model were used in the absence of experimental values on PDTN for boiling point, photodegradation and fugacity. EDTN data were also used to compare with PDTN experimental values for other environmental chemistry endpoints to show similarities between the two chemicals and support the use of PDTN data for mammalian toxicity and ecotoxicity endpoints. Robust summaries of the studies are included in this submission. The Klimisch reliability code was used in the robust summaries. A literature search of online data bases including TOXLINE, HSDB and RTECS was searched. There were no studies identified for EDTN or PDTN.

Physical/Chemical Properties:

The melting point for PDTN is 73-74°C. The boiling point using the EPIWIN model for EDTN is 427°C. The density of PDTN is 1.23 g/cm³. The vapor pressure of PDTN is 1.43×10^{-3} mmHg at 20°C. The log octanol:water partition coefficient (log Kow) of PDTN is -1.3. The water solubility of PDTN is 1.67 g/L. The EPIWIN model for EDTN shows a melting point of 159°C, vapor pressure of 7.54×10^{-8} mmHg at 25°C, a log Kow of -2.17 and water solubility of 1000 g/L. These values for EDTN are consistent with the experimental values of PDTN.

Recommendation: Testing for vapor pressure and water solubility are proposed because the estimated values of EDTN are not consistent with experimental values with PDTN.

Environmental Fate:

AOPWIN was used to estimate the chemical half-life based on an overall OH reaction rate constant. Photodegradation modeling results for EDTN indicate the half-life is estimated to be 4.6 hours.

The hydrolysis half-life of PDTN at pH 4, 7, and 9 at 25°C is estimated to be 5.3, 3.9 and 0.3 years, respectively, based on data at higher temperatures. The EPIWIN model indicates that a hydrolysis half-life cannot be estimated for EDTN at 25°C which is consistent with the experimental data on PDTN.

The EPIWIN Level III fugacity model was used to estimate the distribution of EDTN. The modeling results indicate that EDTN primarily distributes to water and soil. The model will be run again when the EDTN water solubility and vapor pressure data are available.

PDTN was biodegraded 0% at day 28 of a Modified Sturm Test. It is considered not readily biodegradable.

Recommendation: No additional testing is proposed.

Aquatic Toxicity:

The 96 hour LC50 in fish and 48 hour EC50 in *Daphnia magna* for PDTN are greater than 100 mg/L. The 72 hour EC50 for growth inhibition in algae for PDTN is 60 mg/L.

Recommendation: No additional testing is proposed.

Acute Toxicity:

The acute oral and dermal LD50 values in rats for PDTN are greater than 2000 mg/kg. PDTN was not irritating to rabbit skin following a 4 hour exposure and was not sensitizing to guinea pigs in a maximization test.

Recommendation: No additional testing is proposed.

Repeated Dose:

The NOAEL for PDTN in a 28 day oral gavage study in rats was 200 mg/kg/day. At 1000 mg/kg/day, increased liver weight and microscopic changes in the liver were reported.

Recommendation: No additional testing is proposed.

Reproductive/Developmental Toxicity:

There are no reproductive/developmental toxicity data on EDTN or PDTN.

Recommendation: A reproductive/teratology screening study (OECD 421) is proposed for EDTN.

Mutagenicity:

PDTN was not mutagenic in the Ames test or clastogenic in cultured peripheral human lymphocytes in the presence and absence of metabolic activation.

Recommendation: No additional testing is proposed.

TABLE 1: PHYSICAL/CHEMICAL DATA

| CAS # | Chemical (Mol. Weight) | MW | MP °C | BP °C | Vapor pressure (mmHg) | Water Sol. (mg/L) | Log Kow | Phys. Appear. |
|-----------------|---------------------------|-----|------------------|------------------|---------------------------------|-------------------------|--------------------|-------------------------------|
| 5766-67-6 | EDTN (216) | 216 | 159 ^a | 427 ^a | Test | Test | -2.17 ^a | White crystalline solid |
| 110057- 45-9 | PDTN (230) | 230 | 73-74 | No Data | 1.43x10 ⁻³ @ 20°C | 1670 @ 18°C | -1.3 | White crystalline solid |

^a Data from EPIWIN

TABLE 2: SUMMARY OF ENVIRONMENTAL FATE AND ECOTOXICITY DATA

| CAS # | Chemical (Mol. Weight) | Environmental Fate | | | | Ecotoxicity LC50/EC50 (mg/L) | | |
|-----------------|---------------------------|--------------------|---|---------------------------|---|---------------------------------|------------|-------------------------------|
| | | Photodeg (hr.). | Stability in water (25° C) | Biodeg. | Trans./ Distr. | Fish | Invert. | Plants |
| 5766-67-6 | EDTN (216) | 4.6 ^a | No Data | No Data | Primarily to soil/water ^{ab} | No Data | No Data | No Data |
| 110057- 45-9 | PDTN (230) | No Data | 5.3 (pH 4), 3.9 (pH 7) and 0.3 (pH 9) years | Not readily biodegrad. | No Data | >100 | >100 | 60 (growth); 129 (rate) |

^a Data from EPIWIN

^b Will be run again after water solubility and vapor pressure studies

TABLE 3: SUMMARY OF MAMMALIAN TOXICITY DATA

| CAS # | Chemical (Mol. Weight) | | | | | Genetic toxicity | |
|-----------------|---------------------------|---------------------------|--------------------------|--------------|----------|------------------|--------------------|
| | | Acute | Repeated dose | Reproductive | Develop. | Mutagen. | Chrom. Aberr. |
| 5766-67-6 | EDTN (216) | No Data | No Data | Test | Test | No Data | No Data |
| 110057- 45-9 | PDTN (230) | >2 g/kg (oral/ dermal) | NOAEL – 200 mg/kg/day | No Data | No Data | Not mutagenic | Not clastogenic |

Test – OECD 421 study to be done

